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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,905	09/11/2003	Edward T. Wei		7040

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EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/660,905	WEI, EDWARD T.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *8-13 and 18-20* is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *1-7 and 14-17* is/are rejected.

7)☒ Claim(s) *14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/11/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-20 are pending.

Election/Restrictions

Claims 8-13, 18-20 are withdrawn from consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions.

Applicant's election of invention Group I, an eye drop composition comprising one or more doses of a buffered, isotonic ophthalmic solution having therein a pharmaceutically effective amount of a trialkyl phosphine oxide of Formula 1, claims 1-7, and 14-17 in reply filed on 01/22/2007 is acknowledged herein. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The requirement is made FINAL.

Claims 1-7, and 14-17 are examined herein on the merits as they read on the elected invention.

Claim Objections

Claim 14 is objected to because of the following informalities: Claim 14, line 5 recites "wherein R1 is R1". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 5-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "an adjunct to reduce irritancy from the trialkyl phosphine oxide", in claim 1 is vague and indefinite. The specification merely recites sucrose, fructose, dextrose, inositol, carboxymethylcellulose, and hydrocarbon polyols as adjuncts, and does not provide any information as to what other type of compounds can be employed as adjuncts to reduce irritancy from the trialkyl phosphine oxide. See page 18, line 26-page 19, line 7 of instant specification. Thus, one of ordinary skill in the art could not ascertain the metes and bounds as to "an adjunct to reduce irritancy from the trialkyl phosphine oxide", as it is not clear what other compounds this recitation encompasses.

Claims 2, and 16, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "wherein the eye drop composition is substantially non-astringent" in the claims is vague and indefinite. The specification merely recites that "astringents are locally acting pharmacologic agents, which, by precipitating protein, help to clear mucus from the outer surface of the eye", and recites Witch Hazel as an astringent", see page 2, lines 15-17. It is not clear as to what agents other that Witch Hazel which is recited as astringent in the instant specification are excluded in the eye drop composition. Further it is not clear as to what the applicant intends to convey by the

recitation "substantially non-astringent", is it completely i.e 100 % non-astringent or 99.6 % non-astringent.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rowsell et al. (US 4,070,496, PTO-1449), in view of Hecht (Remington, the Science and Practice of Pharmacy, 20th ed. 2000, Chapter 43, pages 821-835, PTO-1449).

Rowsell et al. discloses compositions comprising trialkyl phosphine oxides which read on instantly claimed trialkyl phosphine oxides of Formula 1. See column 1, line 58-column 2 line 24; column 3, Table. It is also disclosed that the trialkyl phoshine oxide compounds therein can be incorporated into eyedrops. See column 5, lines 37-38. An eye lotion comprising 0.005 % of di-isopentyl-sec-butyl phosphine oxide, Boric acid/sodium borate is disclosed. See column 9, EXAMPLE 3. It is also disclosed that compositions comprising trialkyl phosphine oxides are incorporated into a carrier which may be completely inert or which may contain other active ingredients. Carriers depend on the end use of the compositions. Carriers include aqueous or alcoholic solutions; oils and fats; starch; cellulosic material such as sodium carboxymethyl cellulose i.e demulcent/carrier. See column 5, lines 7-18; column 11, line 2. See EXAMPLE 12

wherein compositions comprising n-hexyl-isobutyl-cyclopentyl phosphine oxide in demulcent/carrier such as propylene glycol is disclosed.

Rowsell et al. does not explicitly teach an eyedrop composition comprising buffered isotonic ophthalmic solution having trialkyl phosphine oxide.

Rowsell et al. does not specifically teach instructions to the user for applying the solution indirectly to the eye.

Hecht teaches that a number of requirements such as sterility, clarity, buffer, buffer capacity and pH, tonicity, viscosity must be considered in the preparation of ophthalmic solutions, suspensions, or ointments. It is also taught that the buffer system must be considered with tonicity and comfort in mind. See page 827, right hand column, bottom paragraph. It is taught that ophthalmic preparations should be formulated at a pH equivalent to the tear fluid, and buffer capacity is the key. It is also taught that isotonicity is desirable and important in intraocular solutions. Page 829.

It would have been obvious to a person of ordinary skill in the art to incorporate trialkyl phosphine oxides taught by Rowsell et al. in buffered isotonic eyedrop composition because 1) Hecht teaches that ophthalmic preparations should be formulated at a pH equivalent to the tear fluid, and 2) buffer capacity and tonicity are important factors to be considered in preparing such ophthalmic compositions Thus, one of ordinary skill in the art at the time of invention would have been motivated to employ buffered isotonic ophthalmic solution with the expectation of obtaining a stable eyedrop composition comprising trialkyl phosphine oxide that can be employed for eye care applications.

It would have been obvious to a person of ordinary skill in the art at the time of invention to provide instructions for administering the eye drop composition taught by Rowsell et al. The employment of a pharmaceutical kit or the patient pack comprising pharmaceutical composition in one or more doses and directions for administering the dosage forms are all deemed obvious since they are all within the knowledge and conventional skills of pharmacologist to conveniently assist the user and prescriber for easy dispensary of the medication. Moreover, the inclusion of a package inserts including "indication and use" of the pharmaceutical composition in a pharmaceutical kit is mandated by 21 CFR 201.57 according to *Remington: The Science and Practice of Pharmacy*. It has been established by the court that the content of written instructions was not patentable subject-matter that could be relied upon to overcome a prior art rejection of a biotech kit claim. In re Ngai and Lin (Fed Cir 03-1524, decided March 8, 2004, precedential opinion issued May 13, 2004).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 14 is rejected under 35 U.S.C. 102(b) as being anticipated by Rowsell et al. (US 4,070,496, PTO-1449).

Rowsell et al. discloses compositions comprising trialkyl phosphine oxides which read on instantly claimed trialkyl phosphine oxides of Formula 1. See column 1, line 58-column 2 line 24. It is also disclosed that the trialkyl phoshine oxide compounds therein can be incorporated into eyedrops. See column 5, lines 37-38. An eye lotion comprising 0.005 % of di-isopentyl-sec-butyl phosphine oxide is disclosed. See column 9, EXAMPLE 3; See EXAMPLE 12 wherein compositions comprising n-hexyl-isobutyl-cyclopentyl phosphine oxide in demulcent/carrier such as propylene glycol is disclosed.

Thus, Rowsell et al. anticipates instant claim 14.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rowsell et al. (US 4,070,496, PTO-1449) as applied to claim 14 above, in view of Hecht (Remington, the Science and Practice of Pharmacy, 20th ed. 2000, Chapter 43, pages 821-835, PTO-1449).

Rowsell et al. is as discussed above.

Rowsell et al. does not explicitly teach an eyedrop composition comprising buffered isotonic ophthalmic solution having the particular trialkyl phosphine oxide.

Hecht teaches that a number of requirements such as sterility, clarity, buffer, buffer capacity and pH, tonicity, viscosity must be considered in the preparation of ophthalmic solutions, suspensions, or ointments. It is also taught that the buffer system must be considered with tonicity and comfort in mind. See page 827, right hand column, bottom paragraph. Ophthalmic preparations should be formulated at a pH equivalent to the tear fluid, and buffer capacity is the key. It is also taught that isotonicity is desirable and important in intraocular solutions. Page 829.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular subgenus of trialkyl phosphine oxide compounds in the eye lotion compositions taught by Rowsell et al.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular subgenus trialkyl phosphine oxide compounds in the prior art eye lotion compositions, because Rowsell et al. have broadly covered and encompassed the particular subgenus of trialkyl phosphine oxide compounds, and teaches that the trialkyl phoshine oxide compounds therein can be incorporated into eyedrops

Therefore, one of ordinary skill in the art would have reasonably expected that particular trialkyl phoshine oxide compounds would have same or substantially similar beneficial therapeutic effects and usefulness when incorporated in eye drops, based on the reasonable expectation that structurally similar species usually have similar properties. See, e.g., Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214, and If the claimed invention and the

structurally similar prior art species share any useful property, that will generally be sufficient to motivate an artisan of ordinary skill to make the claimed species, In fact, similar properties may normally be presumed when compounds are very close in structure. Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904, as noted in MPEP 2144.

It would have been obvious to a person of ordinary skill in the art to incorporate trialkyl phosphine oxides taught by Rowsell et al. in buffered isotonic eyedrop composition because 1) Hecht teaches that ophthalmic preparations should be formulated at a pH equivalent to the tear fluid, and 2) buffer capacity and tonicity are important factors to be considered in preparing such ophthalmic compositions Thus, one of ordinary skill in the art at the time of invention would have been motivated to employ buffered isotonic ophthalmic solution with the expectation of obtaining a stable eyedrop composition comprising trialkyl phosphine oxide that can be employed for eye care applications.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Tuesday, Thursday-Friday 8am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shobha Kantamneni, Ph.D
Patent Examiner
Art Unit : 1617

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER